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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/535,509 | 05/18/2005 | Aleardo Koverech | 725.1019 | 7229 |

20311 7590 08/19/2010

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| EXAMINER | |
|---|---|
| BETTON, TIMOTHY E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1627 | |

| NOTIFICATION DATE | DELIVERY MODE |
|---|---|
| 08/19/2010 | ELECTRONIC |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

info@lmiplaw.com

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/535,509 | KOVERECH ET AL. | |
| | Examiner | Art Unit | |
| | TIMOTHY E. BETTON | 1627 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *08 June 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *10-12 and 14-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12 and 14-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

Applicants' Remarks filed on 8 June 2010 have been acknowledged and duly made of record.

### *Response to Arguments*

As an initial matter, the specification/affidavit filed on 15 March 2008 has been reconsidered in view of applicants' issue regarding this purportedly novel limitation drawn to *the improvement comprising a lack of increase of blood testosterone levels*.

An affidavit is a professional opinion and holds no patentable weight in as far as what is already well-established and commonly known in the pertinent art, whether evident or otherwise.

Applicants' remarks drawn to this allegedly unrecognized property of the administration of carnitines are erroneous due to the fact that carnitines do not possess properties that increase testosterone. Instead, carnitine and the various derivatives thereof have the ability to enhance free testosterone (which is only at 2% in the normal male; the other 98% is called bound testosterone).

Therefore, the references as already made of record: Cavazza (USPN 4,474,812) (hereinafter Cavazza ('812)) and Cavazza (USPN 6,245,378) (hereinafter Cavazza ('378)) and De Felice (USPN 3,830,931 in view of De Simone (USPN 6,037, 373) and Xiu (USPN 6,399,116 B1) are proper for what they teach. Applicants' have not sufficiently distinguished which portion of the testosterone index that the limitation '*the improvement comprising a lack of increase of blood testosterone levels'* is directed, i.e., the bound testosterone (98% useless amount) or the free testosterone (2% useful amount).

Applicants' seem to have misconstrued the reason why the tertiary reference Xiu et al. was initially employed. Xiu was employed due to pertinent embodiments drawn specifically to carnitines to the exclusion of all other components. Applicants' attention is directed to pages 7 and 8 of the previous Office Action filed on 18 March 2010 which clearly teach another component, *Rhodiola crenulata* is being the culpable component responsible for the increase in testosterone, not the carnitines or derivatives thereof.

Thus, for the reasons already made of record, the previous 103(a) as filed on 18 March 2010 is maintained.

***Status of the Claims***

Claims 10-12 and 14-18 are pending further prosecution on the merits. Claims 1-9 and 13 are cancelled.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 10-12 and 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cavazza (USPN 4,474,812) (hereinafter Cavazza ('812)) and Cavazza (USPN 6,245,378) (hereinafter Cavazza ('378)) and De Felice (USPN 3,830,931 in view of De Simone (USPN 6,037, 373) and Xiu (USPN 6,399,116 B1).

Cavazza ('812) teaches a novel therapeutic use of L-carnitine and a pharmaceutical L-carnitine-comprising composition [...], whose oral or parenteral administration to elderly subjects brings about an improvement in the biochemical and behavioral parameters peculiar to senility (abstract only).

Cavazza ('812) teaches an embodiment drawn to L- carnitine which teaches the inventive objective of the claimed invention. Though Cavazza teaches embodiments drawn to treatment for senility in association with old-age, Cavazza teaches embodiments which to the skilled artisan would make instant claims 10-12 and 14-18 obvious.

Specifically, Cavazza teaches uses of L-carnitine [which] are already known. For instance, **L-carnitine has been used in the cardiovascular field in the treatment of acute and chronic myocardial ischaemia, angina pectoris, cardiac arrhythmias and insufficiency. In**

**nephrology, L-carnitine has been administered to chronic uraemic patients who are subjected to regular haemodialysis treatment with a view to counteracting muscular asthenia and the onset of muscular cramps. Further therapeutic uses are the restoration of the HDL/LDL+VLDL ratio to normal and in total parenteral nutrition.**

Although the daily dose to be administered depends on the age, weight and general condition of the elderly subject [...] it has been found that, generally, from about 10 to about 30 mg of L-carnitine/kg of body weight/day or an equivalent amount of a pharmacologically acceptable salt thereof, is a suitable dose.

L-carnitine is compounded into the pharmaceutical compositions by using the usual excipients, diluents and adjuvant agents which are well-known in pharmaceutical technology for preparing orally and parenterally administrable compositions. An extensive list of such excipients and adjuvant agents as well as the methods for preparing solid and liquid oral unit dosage forms such as tablets, capsules, solutions, syrups and the like and fluid injectable forms such as sterile solutions, is disclosed in the U.S. Pat. No. 3,830,931 to De Felice.

It has also been found that a pharmaceutical composition in unit dosage form which is particularly suited for the foregoing therapeutic uses comprises from about 500 to about 1,000 mg of L-carnitine.

Cavazza ('812) additionally teach the study of the effects of L-carnitine administration on some biochemical and behavioural parameters in old male rats.

Cavazza does not teach the use of propionyl- L-carnitine and acetyl L- carnitine.

Accordingly, Cavazza ('378) teaches a nutritional supplement for facilitating the adaptation of skeletal muscle in individuals undergoing programs of strenuous exercise and counteracting defatigation and weariness in asthenic individuals is disclosed, which comprises a combination of L-camitine, acetyl L-carnitine and propionyl L-carnitine as basic active ingredients. Optional ingredients comprise isovaleryl L-carnitine, branched-chained aminoacids and creatine and/or phosphocreatine (abstract only).

Cavazza ('378) teaches an extensive embodiment of the indications for L-carnitine (column 2, lines 1-67).

Cavazza ('378) teaches mixtures, combinations and ratio strengths of acetyl and propionyl L-carnitine formulations which encompass the limitations of the instant claims (column 3, lines 64-67; column 4, lines 1-20).

**The skilled artisan would instantly recognize that many of the disorders and disease states are conditions common among geriatric patients.**

De Felice further confirms a well-established use of l-carnitine and carnitine derivatives among geriatric patients (please see Cases 1-12, columns 4-8).

The Cavazza references and De Felice do not specifically teach treatments for hormone disorders caused by andropause, such as the Markush members attributed to side effects and disorders *inter alia* listed in the instant claim 10.

However, De Simone does teach L-acetyl carnitine and L-propionyl carnitine for the treatment of diseases that are related to the ageing subject (e.g. arthritis, asthenia, osteoporosis, etc) (abstract only).

De Simone also teaches an embodiment directed to specific salts of the carnitine formulation (column 2, lines 8-16).

None of the references above directly teach a formulation indicated for the treatment for the decrease in testosterone and/or a decreased libido.

**However, Xiu does teach Rhodiola, preferably Rhodiola crenulata, to treat various conditions and diseases in mammals. Rhodiola crenulata is a Tibetan herb which has been discovered to have highly useful and beneficial properties heretofore unknown. Rhodiola crenulata is especially preferred to enhance blood oxygen levels, to enhance working capacity and endurance, to enhance memory and concentration, to enhance cardiac and cardiovascular function, to provide antioxidant effects, to protect against oxidation, to modulate testosterone and estradiol levels, to modulate sleep, and to enhance sexuability, such as improve sexual performance.**

**Xiu teaches a preferred embodiment drawn to the administration of carnitines in combination with Rhodiola crenulata (col 3, line 19). This adequately encompasses the inventive objective and subject matter limitation disclosed in instant claim 1. Particularly, instant claim 1 cites a method for the treatment of disorders caused by andropause *comprising* administering [...].**

**Specifically, Xiu teach andropause as a disorder indicated for treatment.**

Testosterone is considered to be a male virilizing hormone. Its effects include maintenance of muscle and bone mass, improving and/or enhancing sexual function and psychological well being among others. As males grow older, especially after the age of 35, a slow decline in testosterone levels is observed which is accompanied by symptoms that have

been associated with the condition known as "andropause". Symptoms of andropause include lethargy, depression, lack of sexual desire and function, and loss of muscle mass and strength. (column 4, lines 55-67).

Thus, it would have been *prima facie* obvious to the skilled artisan at the time of invention to incorporate with or combine together the methods and teachings of Cavazza, De Felice, De Simone and Xiu as described above.

The Cavazza references teach methods and intended uses for L-carnitines and derivatives thereof. Cavazza ('812) and ('378) specifically teaches the study of the effects of L-carnitine administration on some biochemical and behavioral parameters in old male rats. The inventive objective in view of the claimed invention is drawn to elderly male subjects. De Felice and De Simone provide the primary motivation to combine via the administration of L-carnitine for an array of diseases associated with aging. Accordingly, Xui teaches embodiments of andropause being treated preferably by L-carnitines, L-carnitine mixtures, and compositions thereof.

The differences between the prior art of record and the claims at issue is directed to the newly amended claim 10, *which discloses the improvement comprising a lack of increase of blood testosterone levels.*

Further reasoning is due to the simple fact that carnitines and amino acids are not art-known or chemically constructed to increase blood testosterone levels.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TIMOTHY E. BETTON whose telephone number is (571)272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB
**/SREENI PADMANABHAN/**

**Supervisory Patent Examiner, Art Unit 1627**